Radiologist and Managment of Hepatic Involvement in Heriditary Tyrosnemia Type 1

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ALGIERS

Hereditary tyrosinemia type 1 (HT1) is an autosomal recessive amino acid disorder.

It is rare (1/100000 births) except in Finland and in Quebec.

According to “the Algerian Association of rare disease” (ADEM) there are nationally, 50 to 60 children affected, the eldest is14 years old.

It occurs due to a deficiency of fumarylacetoacetate hydrolase (FAH), which is a terminal enzyme in Tyrosine metabolism

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Clinical presentation:

Severe liver dysfunction leading to cirrhosis , liver failure ,portal hypertension & HCC

Renal tubular dysfunction & Rickets

Growth failure

Acute Neurologic crisis

Déficit en FAH

Accumulation of FAA in the hépatocytes

Hepatic injury leading to apoptosis

Metabolised to succinyl-acéto-acétate & succinyl-acétone

Interfers with hepatic enzymes activity such :

PBG synthase

p-HPPD

Heme decreased synthesis

Phenyl -ALA [ ]

Increased [ ] tyrosine

++ Blood & urine

Decreqsed qctivity of δ-ALA déshydratase (liver – hématies)

Oncogenesis

Ongoing hepatocyte injury from accumulation of FAA results in increased liver cell turnover

Leading to the formation of regenerative nodules

Within regenerative nodules, some hepatocytes can undergo further gnomic changes with atypia and hence progress to liver cell dysplasia.

Nodules increase in size and cellularity, giving rise to the formation of dysplastic nodules and, finally, HCC

Diagnosis

Biochemical Findings :

- **In blood** : increased concentration of succinylacetone, tyrosine,methionine, and phenylalanine
- **In Urine**: elevated concentration of succinyl choline, tyrosine metabolites, and the compound δ-ALA.

Molecular genetic testing :

- molecular genetic testingidentification of biallelic pathogenic variants in FAH

Mangement / Treatment

Nitisinone (Orfadin®):

Blocks parahydroxyphenylpyruvic acid dioxygenase (p-HPPD), the second step in the tyrosine degradation pathway, and prevents the accumulation of FAA and its conversion to succinylacetone

Low tyrosine diet.

Nitisinone increases blood concentration of tyrosine, necessitating a low-tyrosine diet to prevent tyrosine crystals from forming in the cornea.

Liver Transplantation: Only Definitive Treatment

RADIOLOGIST AND MANAGEMENT OF TYROSINEMIA TYPE 1

« As clinically indicated »

Biopsy! is **NOT** indicated in the Diagnosis of **HCC**!

The main imaging challenge is to distinguish Regenerative, Siderotic & Low Grade Dysplasic Nodules from small **HCC**

Imaging Modalities

Doppler-Ultrasonography:

First-line examination to detect liver lesions

Technique:

- Doppler
- B mode: 5-7 Mhz probe
  High frequency linear probe

MRI

Modality of choice, important for the assessment of cirrhosis and its complications.

Faster sequences now allow high-quality liver imaging

Automated contrast detection methods with faster sequences allow capture of the arterial phase, essential for the detection of HCC.

The lack of Ionizing Radiation permits routine use of MRI screening.

Protocol

Scout/ Coronal T2 HASTE

Axial T2 SE et STIR

Axial T1 In/Opposed phase

Axiale DWI (B 0 - 50 - 400 - 1000)

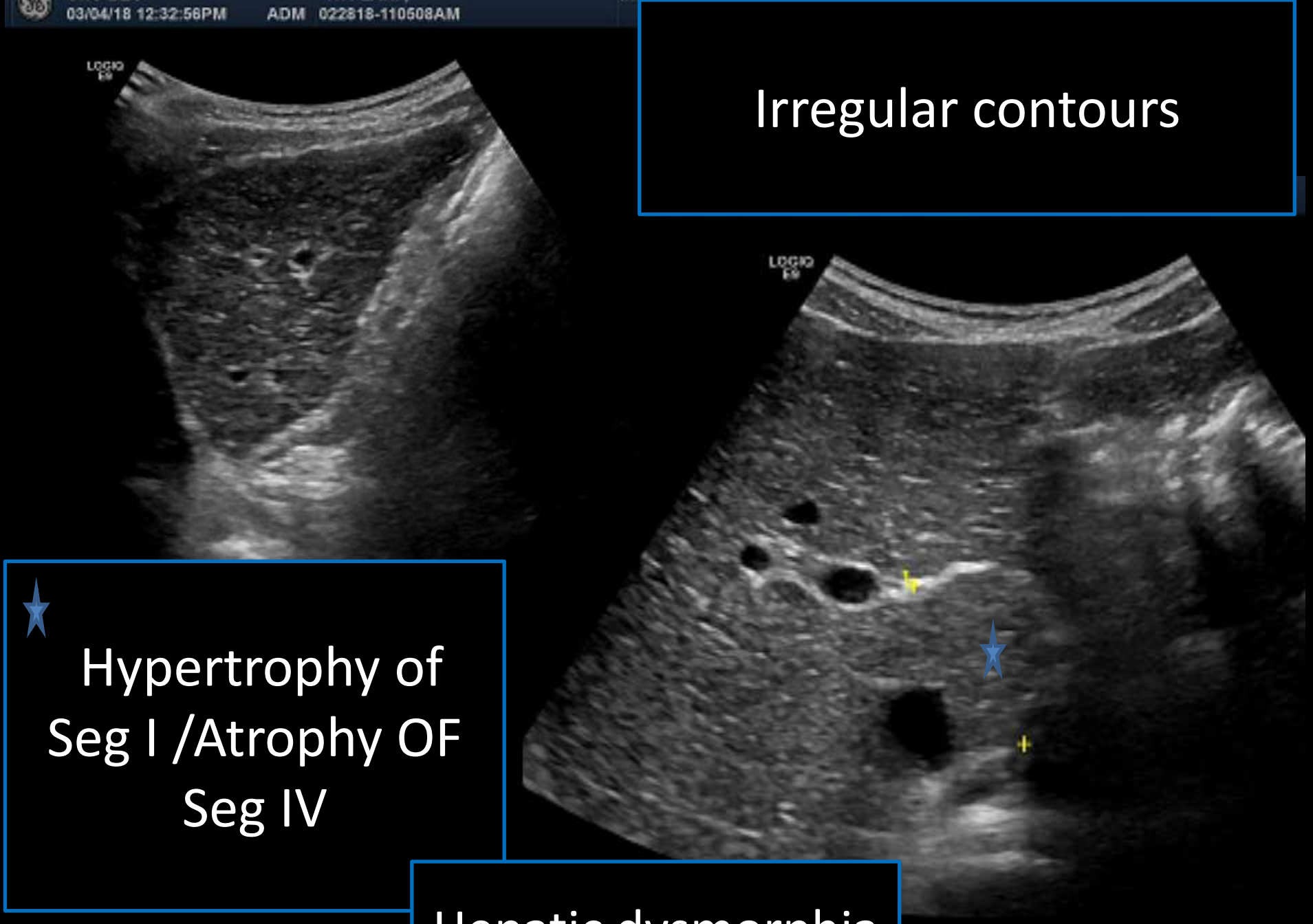
Axiale VIBE :

- Basal
- Arterial phase
- Portal phase
- Late phase 3 mn

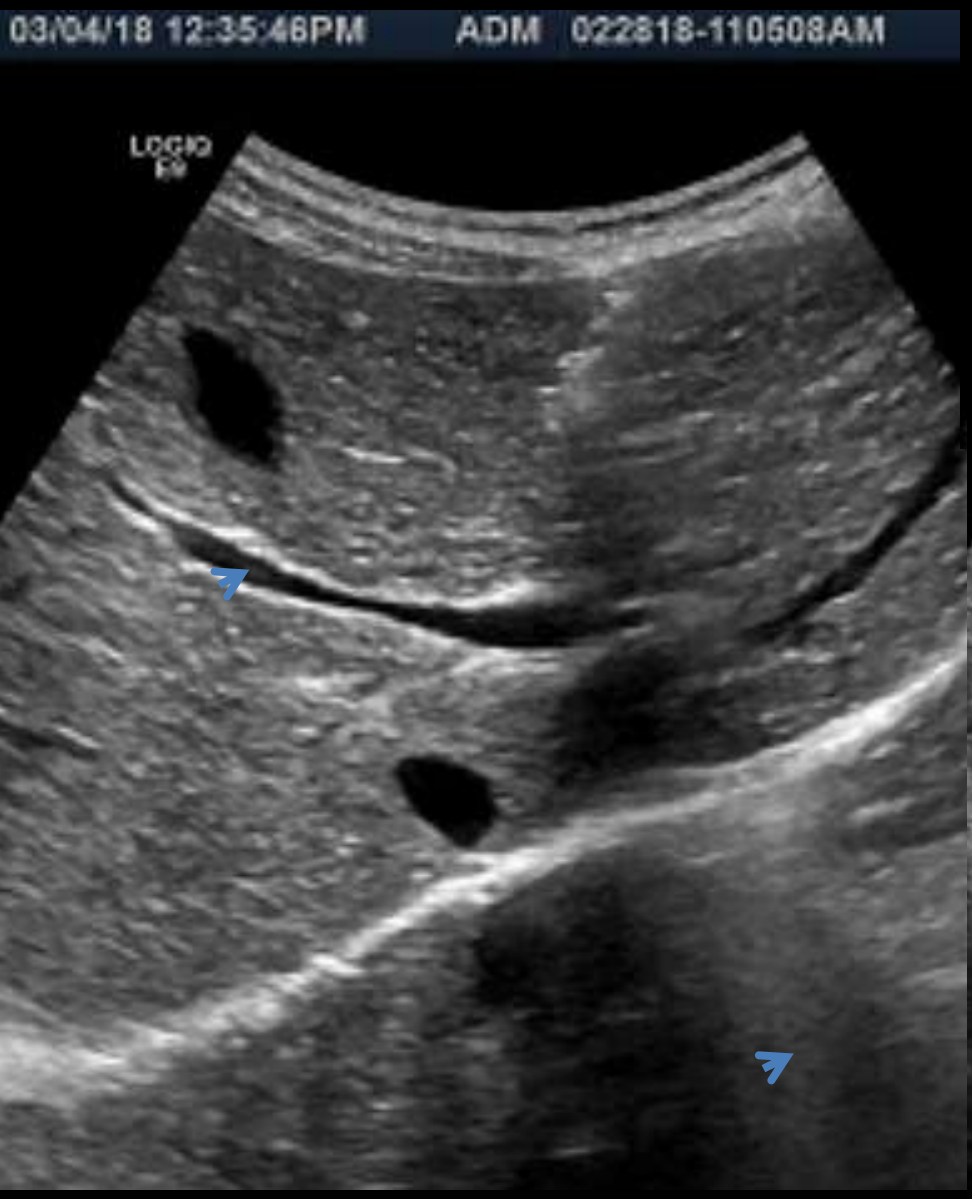
FINDINGS

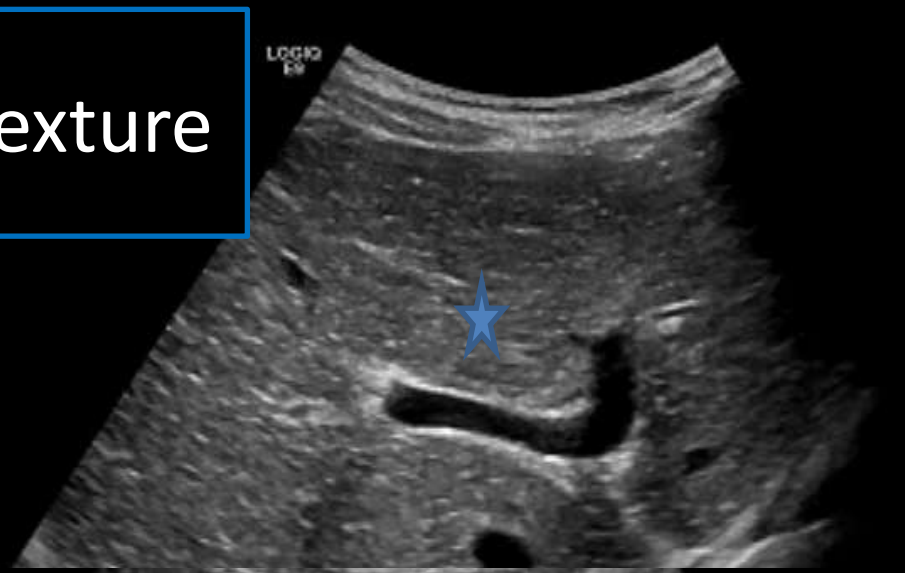
US

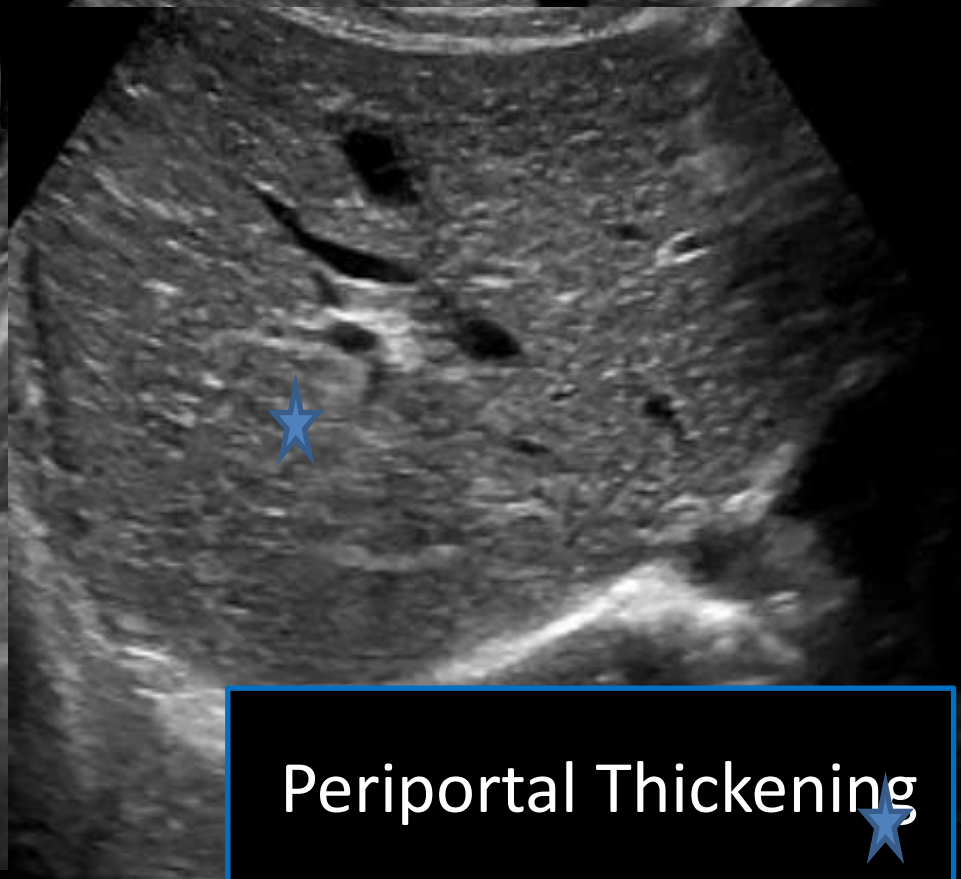
- Irregular Suface (nodularity)
- Overall Coarse and Heterogeneous Parenchyma
- Hepatic Dysmorphia
- Periportal Thickening (fibrosis)


03/04/18 12:32:56PM ADM 022818-110508AM
Irregular contours
Hypertrophy of Seg I /Atrophy OF Seg IV
Hepatic dysmorphia

Coarse heterogeneous echotexture







Periportal Thickening

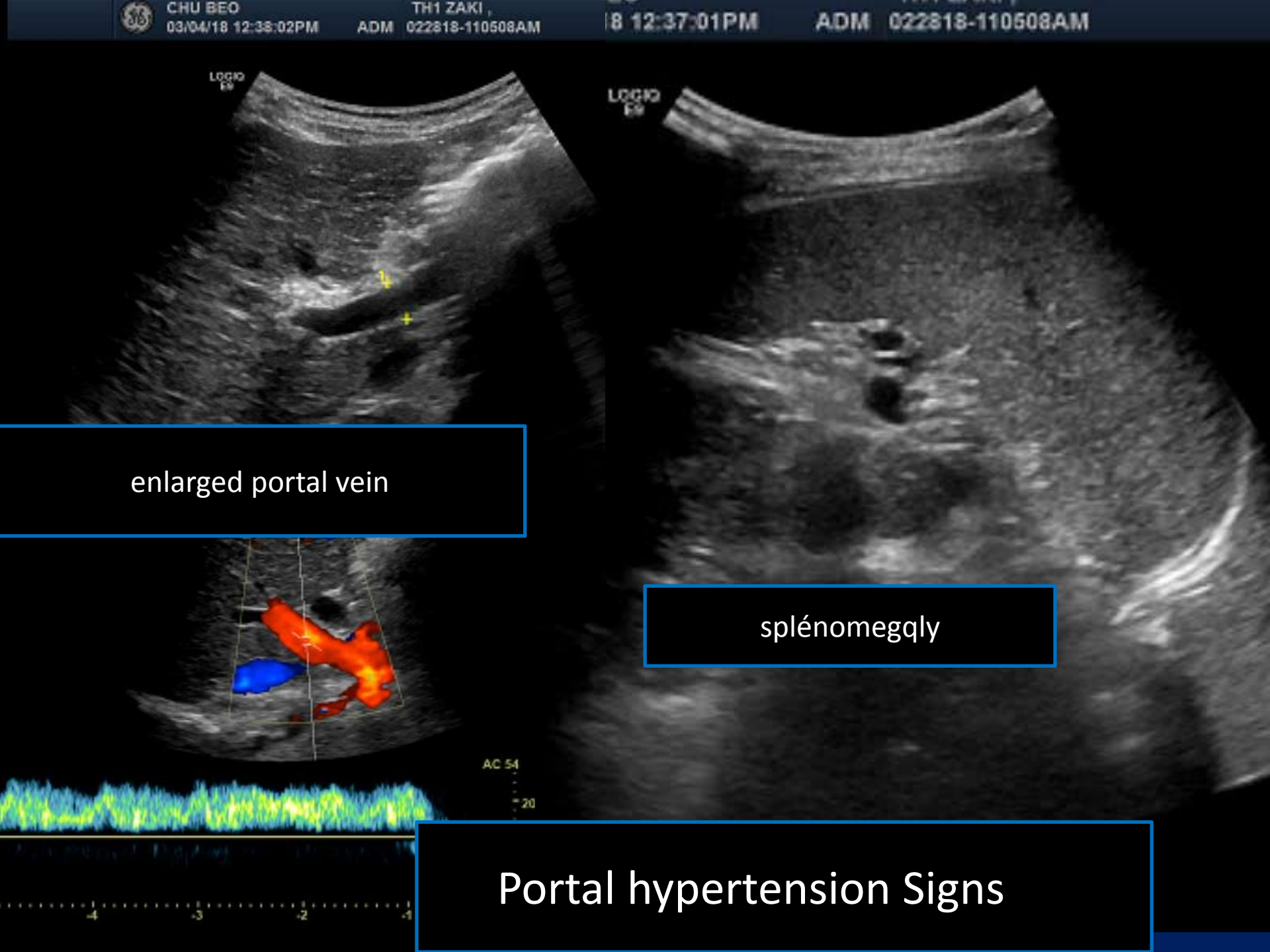
US /Doppler

Signs of Portal Hypertension:

Doppler flow changes

- Eenlarged portal vein: >13 mm
- Slow portal venous flow <15 cm/sec
- Reversal or to-and-fro portal venous flow
- Portal venous thrombosis +/- cavernous transformation
- Enlarged SMV and splenic vein: >10 mm
- Portosystemic collaterals
- Portalisation of hepatic vein waveform

Splenomegaly
Ascites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enlarged portal vein
splénomegqly
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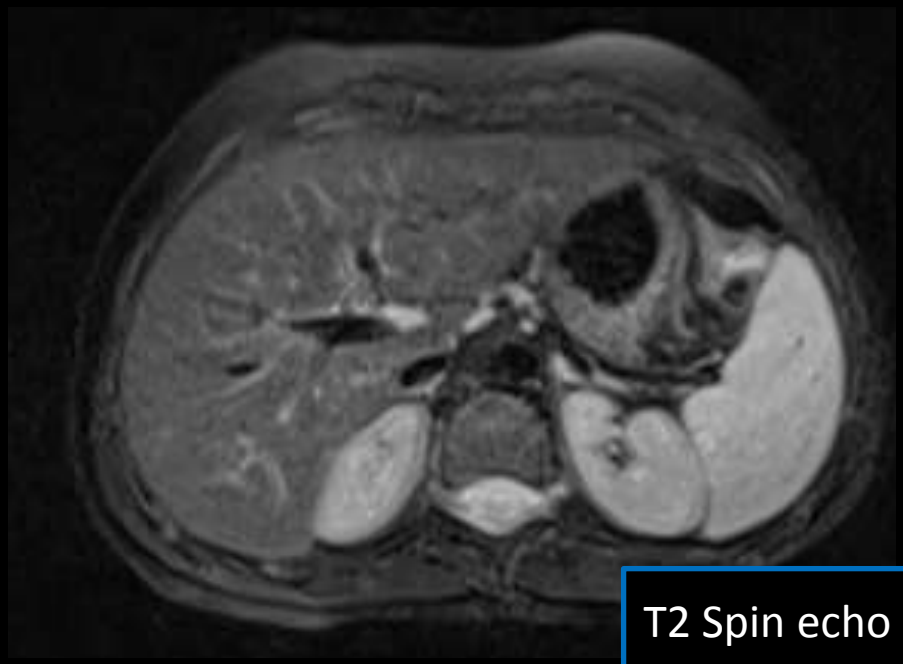
Portal hypertension Signs

MRI

MRI findings include morphologic changes
(same as on CT and US)

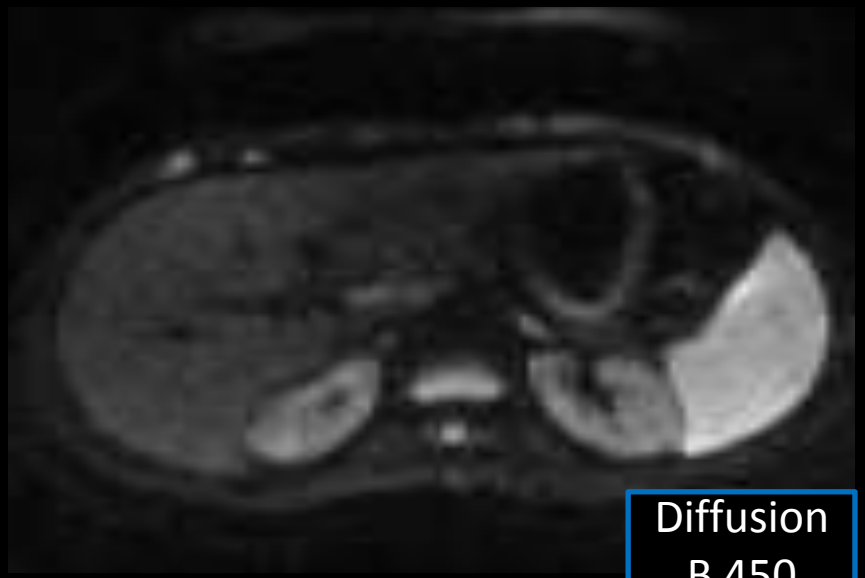
MRI has a significant role in screening cirrhotic livers for small HCCs



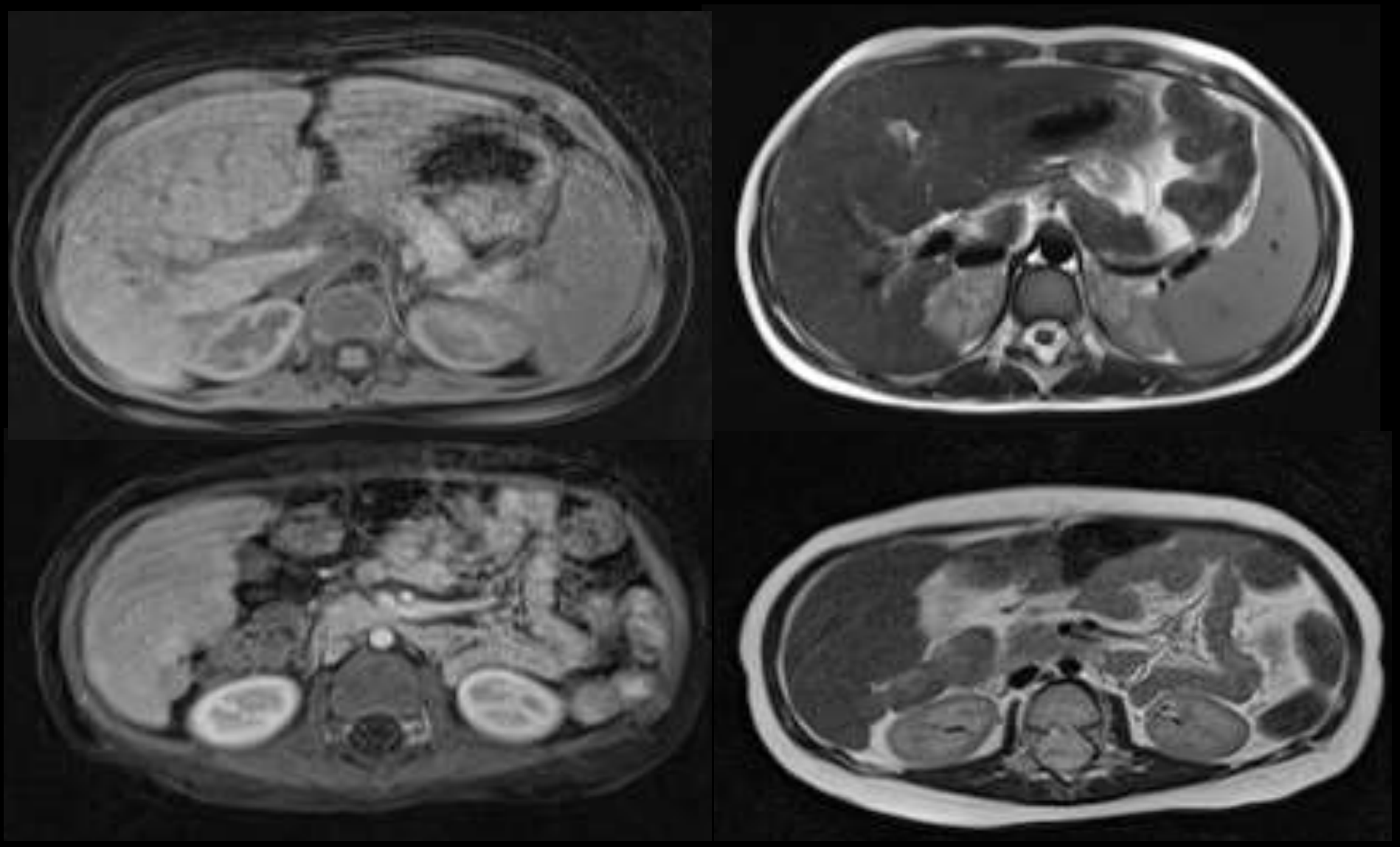
T2 Spin echo

T1 vibe arterial phase

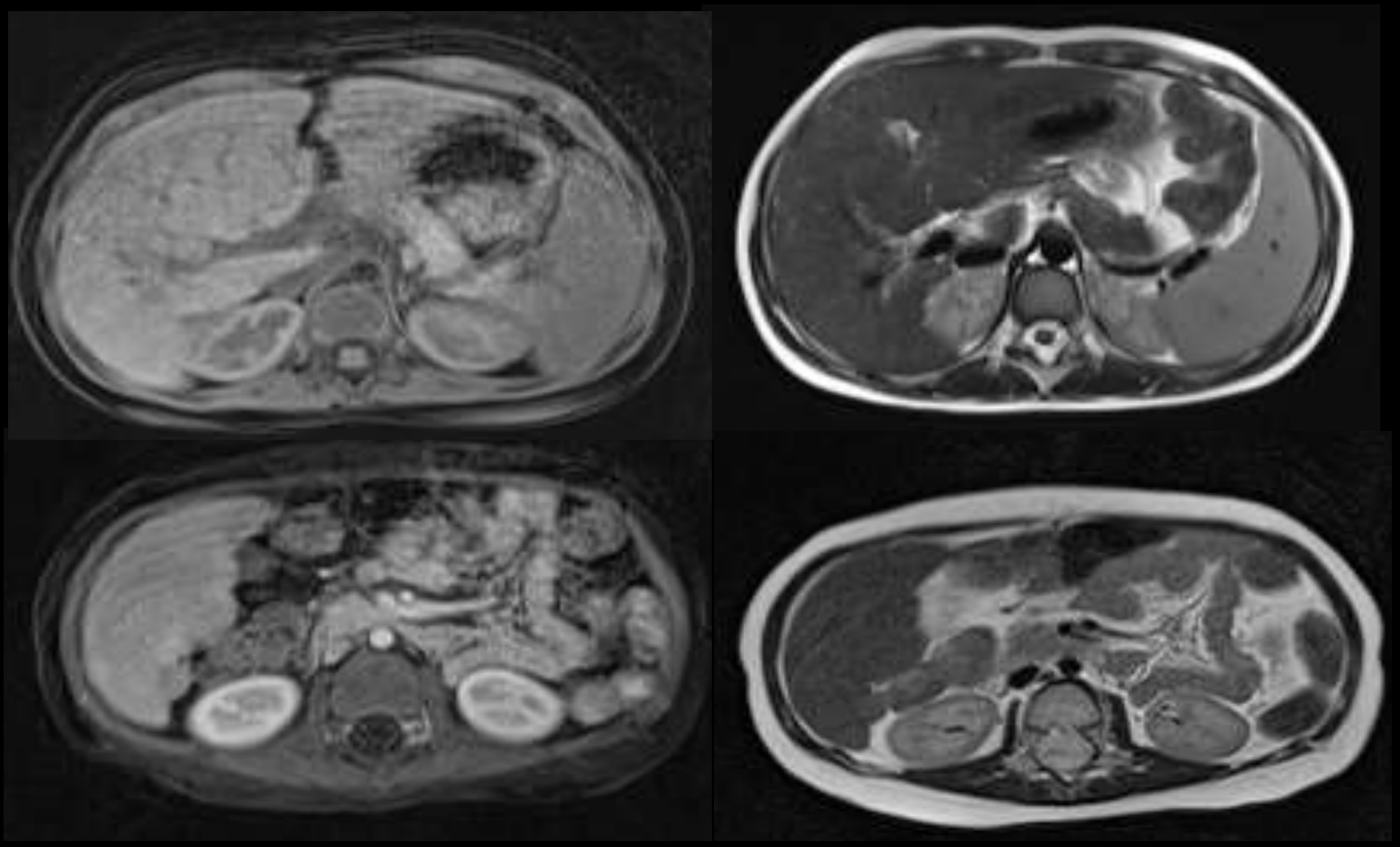
No nodular enhancement in arterial phase



Diffusion
B 450



Chronic Hepatopathy: Irregular Contours , Heterogeneous Signal
No nodular enhancement in arterial phase



Chronic hepatopathy

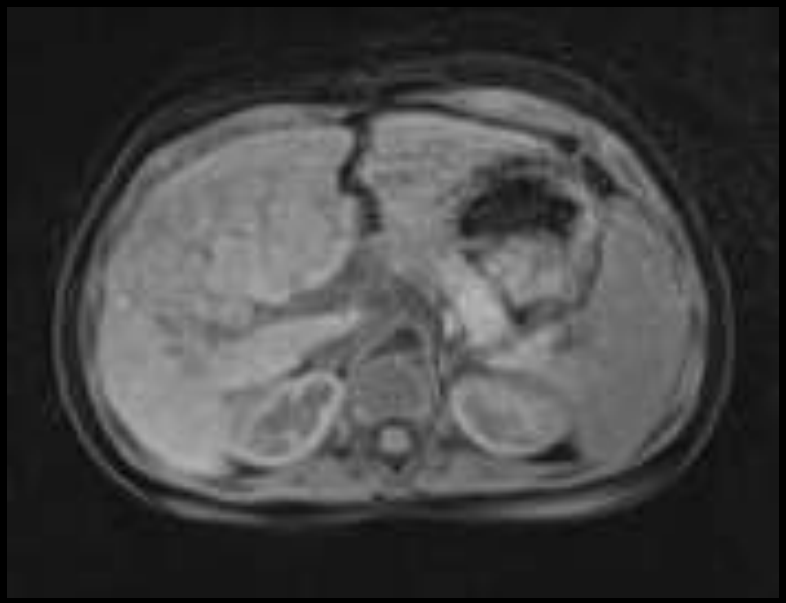
NODULES

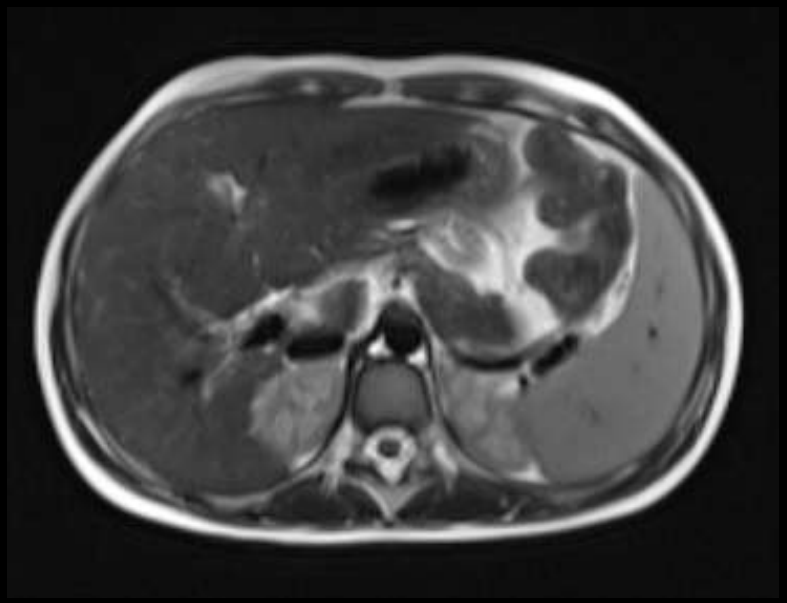
Regenerative Nodules (or Siderotic)

Dysplastic Nodules

Hepatocellular Carcinoma

Regenerative & Siderotic Nodules)

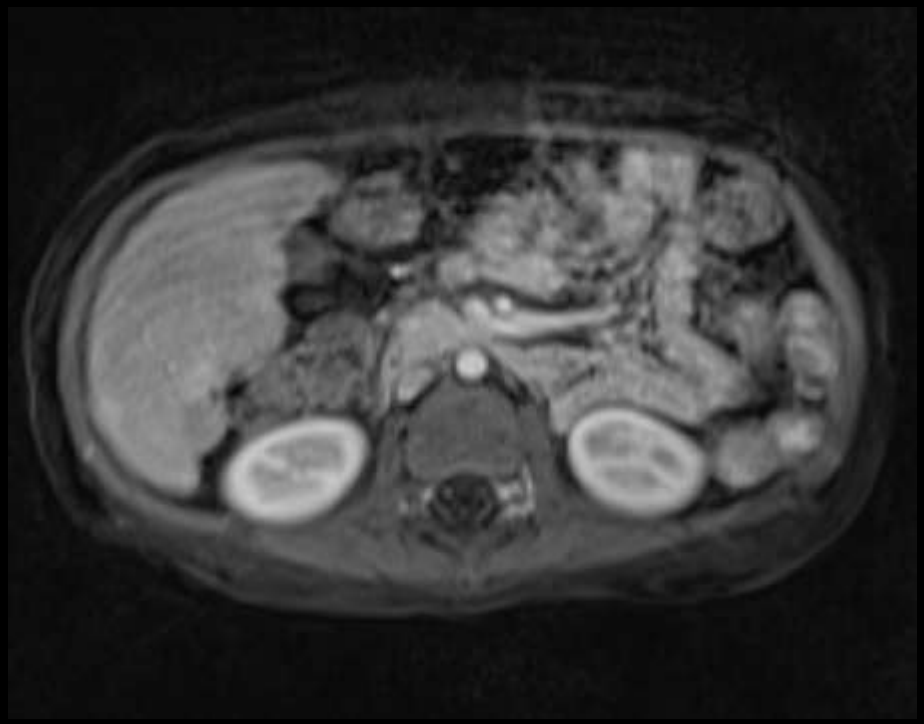


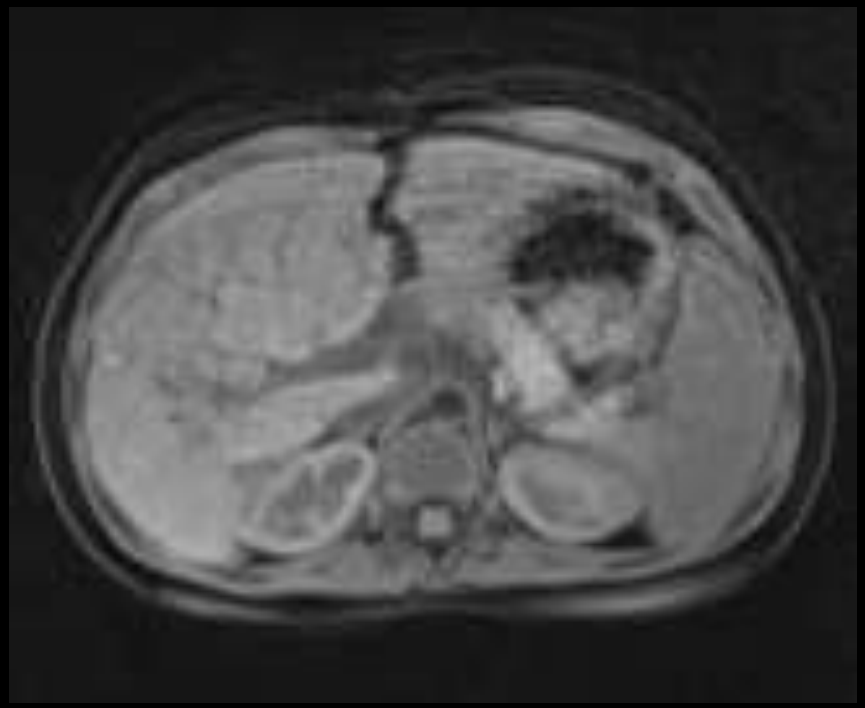


T1 : variable: Usu. Iso
Occa: Hyper Intense

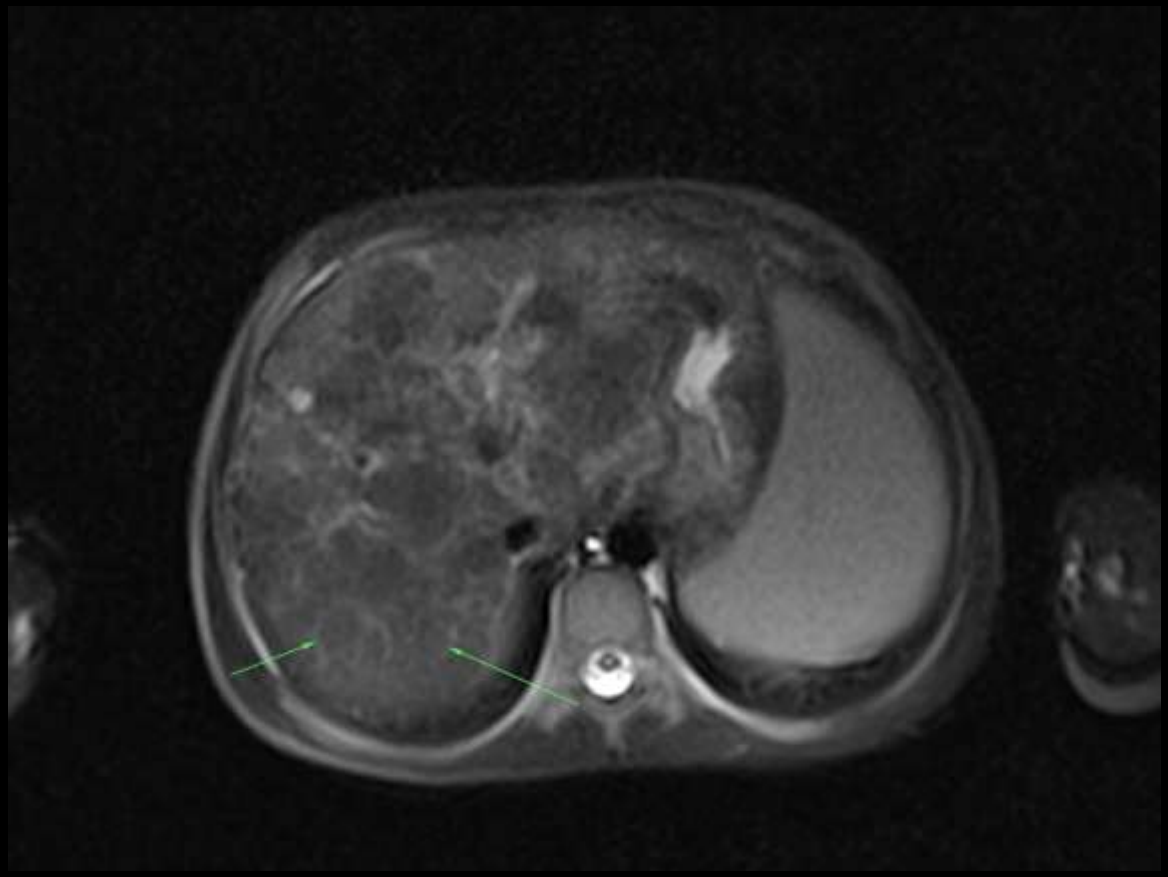
T2 : Isointense
hypointense if siderotic

Regenerative nodules (or cirrhotic nodules)

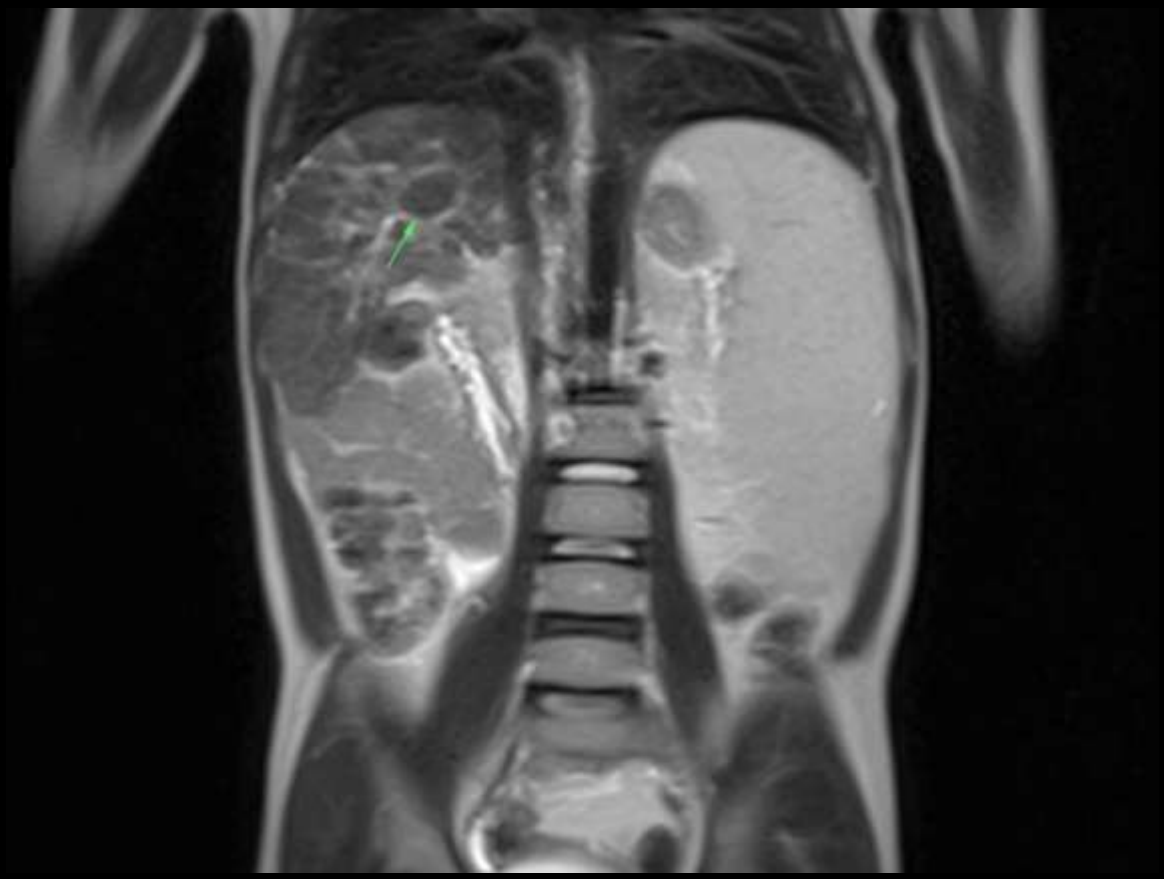




T1 + Gado : No early enhancement and washout
As most Supply is from the Portal vein



Regeneratives nodules isointense on T2



Siderotic nodule , hypointense on T2

Dysplastic Nodule

May be of Low or High grade, and thus have variable appearances :

Low-grade nodules will resemble regenerative nodules

High-grade nodules will resemble HCCs

Hepatocellular Carcinoma (HCC)

T1 C+ (Gd):

Arterial phase enhancement and washout

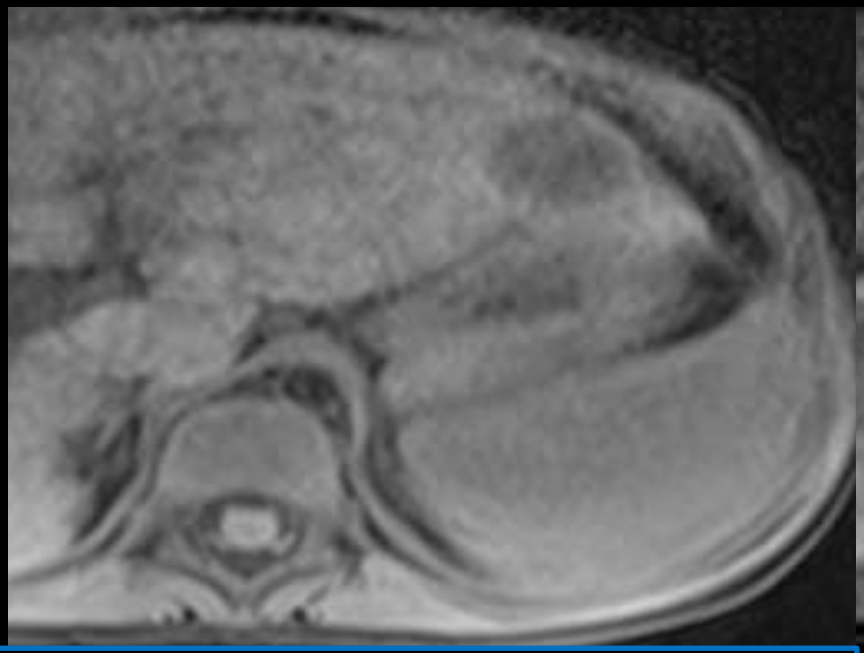
Late enhancing capsule

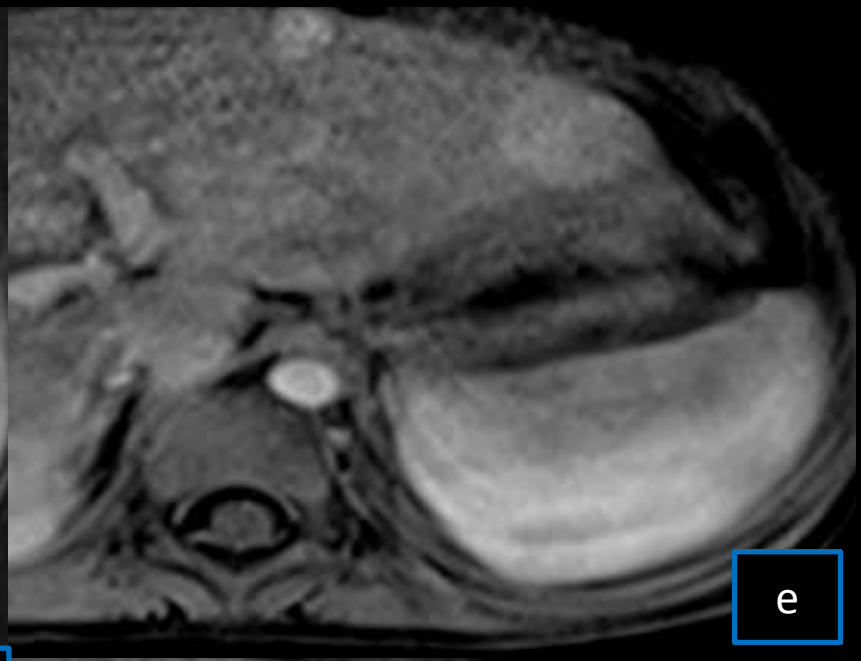
Growth in the interval between studies

T2:

Typically mildly or moderately hyperintense

MR angiography may also be used to asses portal vein patency and portosystemic collaterals.



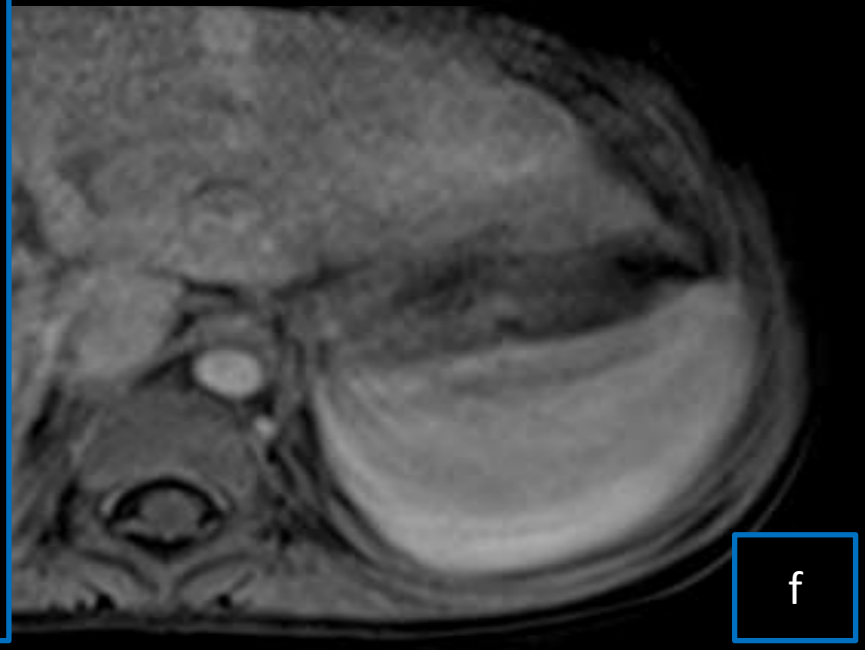


e

Segment 2 nodule: Hypointense nodule on fast T 1 with fat Sat

Arterial phase enhancement and washout (e)

Late enhancing capsule (f).



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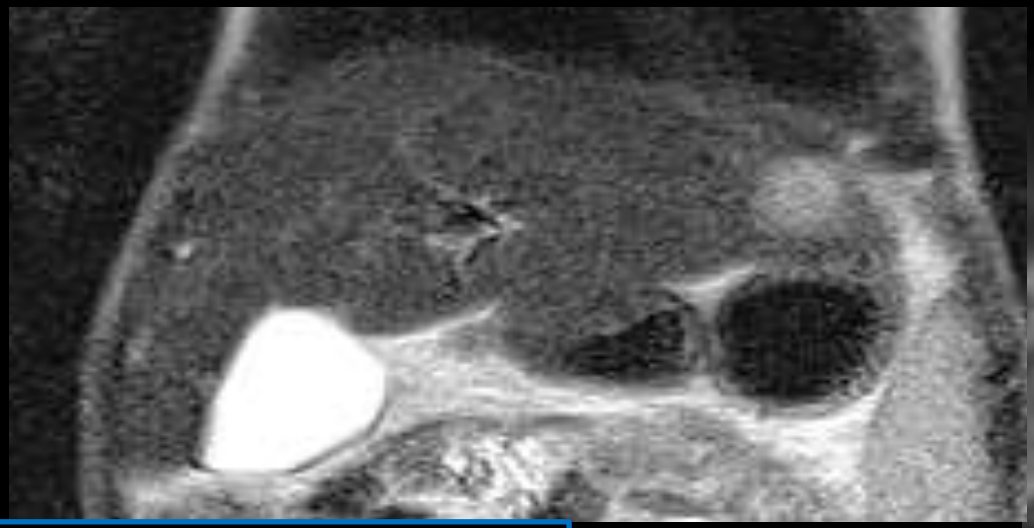
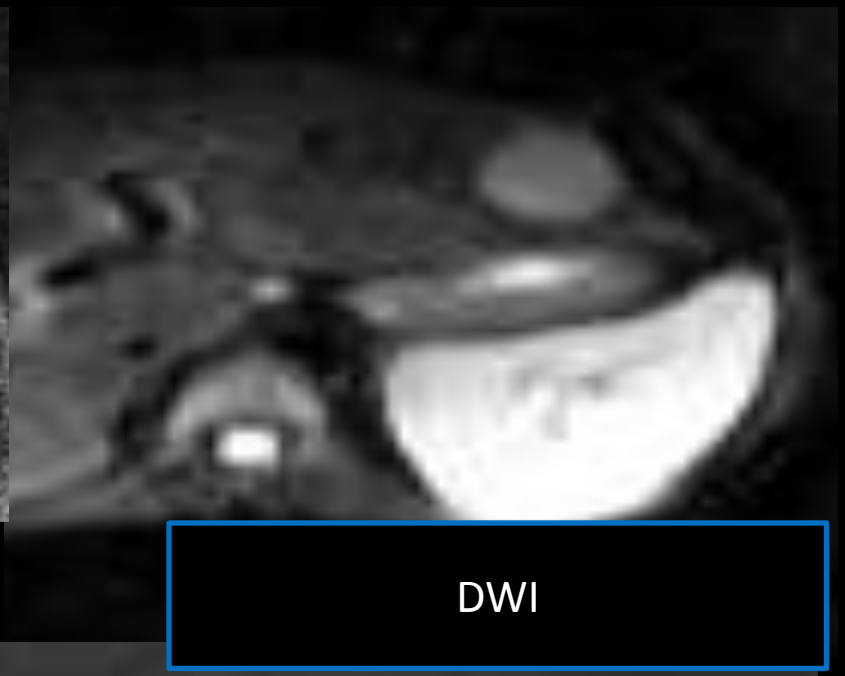
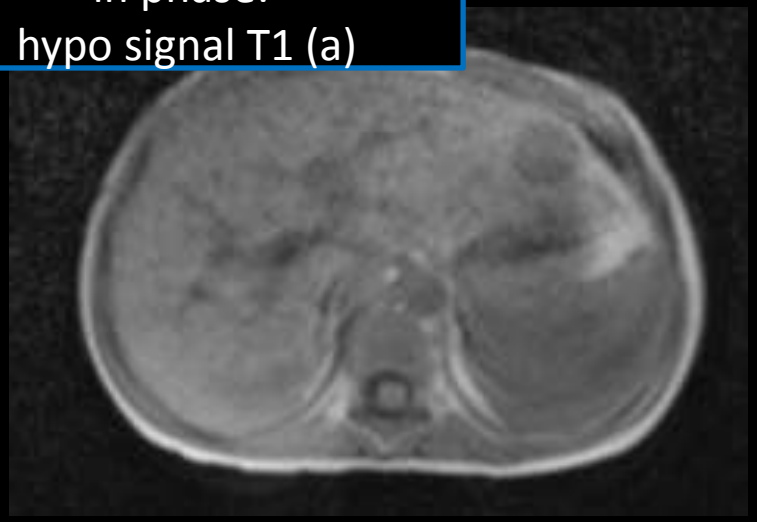


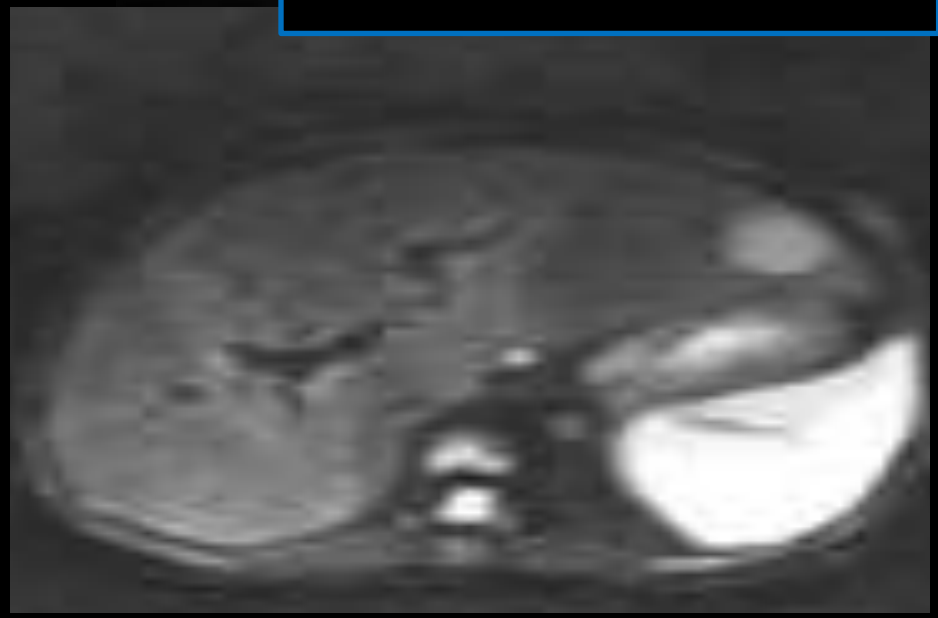
typical Hypersignal T2



DWI

in phase:
hypo signal T1 (a)





Conclusion:

Tyrosinemia is a very rare metabolic disease but should not be ignored as it can result in hepatic and renal failure.

Since biopsy is not conducted , MRI plays a crucial role in diagnosing hepatocellular carcinoma.

Transplantation is the best available treament for tyrosinemia in cases of advanced cirrhosis and hepatic failure with or without Hepatocellualr carcinoma.

THANK YOU

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References

-Hereditary tyrosinemia type 1 from a single center in Egypt: clinical study of 22 cases Hanaa El-Karaksy, Mona Fahmy, Mona El-Raziky, Nehal El-Koofy, Rokaya El-Sayed, Mohamed S. Rashed, Hasan El-Kiki, Ahmad El-Hennawy, Nabil Mohsen

-imaging features of type 1 hereditary tyrosinemia: a review of 30 patients Jos6e Dubois Laurent Garel Heidi Patriquin Khazal Paradis Sylviane Forget Denis Filiatrault Andr6e Grignon

Imaging spectrum of tyrosenimia: A rare metabolic disease entity. S. Solanki, K. Dave; Ahmedabad/IN